

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Lisa C. McConlogue et al.

Application No.: Unassigned

Filed: Herewith

For: TRANSGENIC ANIMALS  
HARBORING APP ALLELE HAVING  
SWEDISH MUTATION

Examiner: Crouch, D.

Art Unit: 1632

**INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 09/838,556, filed April 18, 2001 and issued as US Patent 6,586,656 on July 1, 2003 (Attorney Docket No. 015270-000424US). It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

The Examiner is advised that two related patents, US 5,612,486 and US 5,850,003, from which the present application derives priority have been subject to litigation (Elan Pharmaceuticals, Inc. and Athena Neurosciences, Inc. v. Mayo Foundation for Medical Education and Research, No. C99-4464 WHA (BZ) in the United States District Court for the Northern District of California). In its April 26, 1999 complaint in this suit, Elan alleged that

Mayo willfully infringed, contributorily infringed, or induced the infringement of United States Patent Nos. 5,612, 486 and 5,850,003. The complaint sought a judgment of patent infringement, unspecified actual and treble damages, an injunction, attorneys' fees, and costs of suit. Mayo's May 14, 1999 Answer and Counterclaim denied that the patents were infringed, alleged the patents were invalid and unenforceable due to inequitable conduct and unclean hands and sought a declaratory judgment of noninfringement, invalidity, or unenforceability due to inequitable conduct and unclean hands, an injunction precluding enforcement of the patent, and attorneys' fees and costs of suit.

On April 27, 2000, Mayo moved for summary judgment on the grounds of anticipation. On June 15, 2000, the District Court issued an Order Granting Defendant's Motion for Summary Judgment of Anticipation and entered Judgment in favor of Mayo. In its Order, the District Court found United States Patent Nos. 5,612, 486 and 5,850,003 invalid as being anticipated by United States Patent No. 5,455,169. Notwithstanding the fact that Applicants submitted the '169 patent in the prosecution of the '486 patent and the Examiner indicated her consideration of the '169 patent by initialing the IDS and issuing a Supplemental Notice of Allowance, Mayo alleged that Elan and Athena had committed inequitable conduct by withholding the '169 patent. Mayo presented the crux of its argument and evidence of inequitable conduct to the District Court in its motion for summary judgment. However, the District Court found in an Order Denying Mayo's Ex Parte Motion To Stay Deadline For Motion for Attorney's Fees that "[t]he present record would not support a finding that this was an exceptional case under 35 U.S.C. 285. Mayo will not be allowed to re-open the judgment to submit new material showing that there was fraud on the PTO or on any other ground." On July 18, 2000, Elan's Appeal of the district court's decision was docketed in the United States Court of Appeals for the Federal Circuit as Case No. 00-1467. The Federal Circuit has issued a decision reversing the district court's decision. However, the Federal Circuit's decision has been vacated pending en banc rehearing. No en banc decision has yet issued.

As provided for by 37 CFR 1.97(g) and (h), no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information, and no inference should be made that the information and references cited are, or are considered to be material to patentability because they are in this statement. No inference should be made that the information and references cited are prior art merely because they are in this statement.

Applicant believes that no fee is required for submission of this statement. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Joe Liebeschuetz  
Reg. No. 37,505

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<p>Substitute for form 1449/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p><i>(use as many sheets as necessary)</i></p>				<p><b>C mplete if Known</b></p>	
<p>Application Number</p>		<p>Unassigned</p>			
<p>Filing Date</p>		<p>Herewith</p>			
<p>First Named Inventor</p>		<p>McLonlogue, Lisa C., et. al.</p>			
<p>Art Unit</p>		<p>1632</p>			
<p>Examiner Name</p>		<p>Crouch, D.</p>			
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<p>of</p>		<p>14</p>			

## U.S. PATENT DOCUMENTS

Examiner Signature		Date Considered	
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**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Kind Codes of U.S. Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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		Examiner Name	Crouch, D.
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		Attorney Docket Number	
		015270-012100US	

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
AW	EP	123 527			10-31-1984			<input type="checkbox"/>
AX	EP	171 496			11-21-1991			<input type="checkbox"/>
AY	EP	173 494			03-05-1986			<input type="checkbox"/>
AZ	EP	184 187			06-03-1992			<input type="checkbox"/>
BA	EP	444 856			09-03-1997			<input type="checkbox"/>
BB	JP	87-100291						<input type="checkbox"/>
BC	WO	86/01533			03-13-1986			<input type="checkbox"/>
BD	WO	87/02671			05-07-1987			<input type="checkbox"/>
BE	WO	90/12870			11-01-1990			<input type="checkbox"/>
BF	WO	90/12871			11-01-1990			<input type="checkbox"/>
BG	WO	91/16628			10-31-1991			<input type="checkbox"/>
BH	WO	91/19810			12-26-1991			<input type="checkbox"/>
BI	WO	92/13069			08-06-1992			<input type="checkbox"/>
BJ	WO	92/00521			01-09-1992			<input type="checkbox"/>
BK	WO	92/09699			06-11-1992			<input type="checkbox"/>
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BO	WO	93/01817			03-03-1993			<input type="checkbox"/>
BP	WO	94/23049			10-13-1994			<input type="checkbox"/>
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BR	WO	94/10569			05-11-1994			<input type="checkbox"/>
BS	WO	94/01772			01-20-1994			<input type="checkbox"/>
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## Complete if Known

Application Number	Unassigned
Filing Date	Herewith
First Name Inventor	McLonlogue, Lisa C., et. al.
Art Unit	1632
Examiner Name	Crouch, D.

Attorney Docket Number 015270-012100US

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	BT	"Alzheimer's Assult," <u>ScienceScope</u> , pg. 1059 (2/28/92).	
	BU	Abraham et al., "A calcium-activated protease from Alzheimer's disease brain cleaves at the N-terminus of the amyloid $\beta$ -protein" <u>Biochem. Biophys. Res. Comm.</u> , 174:790-796 (1991).	
	BV	Ali et al., "More Transgenic Mouse Studies of Alzheimer Amyloid Precursor (APP) Proteins and Derivatives," <u>Society for Neuroscience Abstracts</u> , 18(2):abstract 616.8, from 22nd annual meeting in Anaheim, CA 10/25-30/92.	
	BW	Allison et al., "Diabetes in transgenic mice resulting from over-expression of class I histocompatibility molecules in pancreatic $\beta$ cells," <u>Nature</u> , 333:529-533 (1988).	
	BX	Antal et al., "Animal Models of Alzheimer's, Parkinson's and Huntington's Disease. A Minireview," <u>Neurobiology</u> , 1(2):101-122 (1993).	
	BY	BONADIO et al., "Transgenic Mouse Model of the Mild Dominant Form of Osteogenesis Imperfecta," <u>PNAS</u> , 87:7145-7149 (1990).	
	BZ	BUXBAUM et al., "Expression of APP in Brains of Transgenic Mice Containing the Entire Human App," <u>Gene</u> , 197(2):639-645 (1993).	
	BAA	Cai et al., "Release of excess amyloid beta protein from a mutant amyloid beta protein precursor" <u>Science</u> 259:514-516 (Jan. 22, 1993).	
	CA	Cai et al., "Release of Excess Amyloid $\beta$ Protein Precursor." <u>Science</u> , 259:514-516 (1993).	
	CB	Ceballos-Picot et al., "Neuronal-specific expression of human copper-zinc superoxide dismutase gene in transgenic mice: animal model of gene dosage effects in Down's syndrome," <u>Brain Research</u> , 552:198-214 (1991).	
	CC	Chartier-Harlan et al., "Early onset Alzheimer's disease caused by mutations at codon 717 of the $\beta$ -amyloid precursor protein gene" <u>Nature</u> , 353:844-846 (1991).	
	CD	Citron et al., "Mutation of the beta-amyloid precursor protein in familial Alzheimer's Disease increases beta-protein production" <u>Nature</u> , 360:672-674 (Dec. 17, 1992).	
	CE	Citron et al., "Mutation of the $\beta$ -amyloid precursor protein in familial Alzheimer's disease increases $\beta$ -protein production," <u>Nature</u> , 360:672-674 (1992).	

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	CF	Cotton, R.G.H., "A G to C Transversion in Codon 258 of the $\alpha$ -Subunit of $\beta$ -Hexosaminidase A in an Infant Tay-sachs Disease Patient," <u>Human Mutation</u> , 2:496-497 (1993).	
	CG	Crawford et al., "Alzheimer's Disease Untangled," <u>BioEssays</u> , 14(11):727-734 (1992).	
	CH	De Strooper et al., "Study of the Synthesis and Secretion of Normal and Artificial Mutants of Murine Amyloid Precursor Protein (APP): Cleavage of APP Occurs in a Late Compartment of the Default Secretion Pathway," <u>Journal of Cell Biology</u> , 121(2):295-304 (1993).	
	CI	Dovey et al., "Cells with a familial Alzheimer's disease mutation produce authentic $\beta$ -peptide," <u>NeuroReport</u> , 4:1039-1042 (1993).	
	CJ	Epstein et al., "Transgenic mice with increased Cu/Zn-superoxide dismutase activity: Animal model of dosage effects in Down syndrome," <u>PNAS</u> , 84:8044-8048 (1987).	
	CK	Erickson, D., "Model Mice, Transgenic animals aid Alzheimer's research," <u>Scientific American</u> , September 1991.	
	CL	Esch et al., "Cleavage of amyloid $\beta$ peptide during constitutive processing of its precursor" <u>Science</u> , 248:1122-1124 (1990).	
	CM	Estus et al., "Potentially amyloidogenic, carboxyl-terminal derivatives of the amyloid protein precursor" <u>Science</u> , 255:726-728 (1992).	
	CN	Felsenstein et al., "Transgenic Rat and In-Vitro Studies of $\beta$ -Amyloid Precursor Protein Processing," pgs. 401-409 from <u>Alzheimer's and Parkinson's Disease</u> , edited by Hanin, I., Plenum Press, New York, (1995).	
	CO	Fidani et al., "Screening for mutations in the open reading frame and promoter of the $\beta$ -amyloid precursor protein gene in familial Alzheimer's disease: identification of a further family with APP717 Val $\rightarrow$ 11e," <u>Human Molecular Genetics</u> , 1(3):165-168 (1992).	
	CP	Fisher et al., "Expression of the amyloid precursor protein gene in mouse oocytes and embryos," <u>PNAS</u> , 88:1779-1782 (1991).	
	CQ	Forss-Petter et al., "Transgenic mice expressing $\beta$ -galactosidase in mature neurons under neuron-specific enolase promoter control" <u>Neuron</u> , 5:187-197 (1990).	
	CR	Francis et al., "Animal and Drug Modelling for Alzheimer Synaptic Pathology," <u>Progress in Neurobiology</u> , 39:517-545 (1992).	

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	CS	Fraser et al., "Biochemistry of Alzheimer's Disease Amyloid Plaques," <u>Clin. Biochem.</u> , 26:339-349 (1993).	
	CT	FUKAMIZU et al., "Chimeric Renin-angiotensin System Demonstrates Sustained Increase in Blood Pressure of Transgenic Mice Carrying Both Human Renin and Human Angiotensinogen Genes," <u>Journal of Biological Chemistry</u> , 268(16):11617-11621 (1993).	
	CU	Fukuchi et al., "Intestinal $\beta$ -Amyloidosis in Transgenic Mice," abstract 421.16, <u>Society for Neuroscience Abstracts</u> , 19:1035 (1993).	
	CV	Fukuchi et al., "Transgenic Animal Models for Alzheimer's Disease," <u>Annals of the New York Academy of Sciences</u> , 695:217-223 (1993).	
	CW	Fuminori et al., "Transgenic mice for the amyloid precursor protein 695 isoform have impaired spatial memory," <u>NeuroReport</u> , 2:781-784 (1991).	
	CX	Gallagher et al., "Animal models of normal aging: relationship between cognitive decline and markers in hippocampal circuitry," <u>Behavioural Brain Research</u> , 57:155-162 (1993).	
	CY	GANDY et al., "Amyloidogenesis in Alzheimer's Disease: Some Possible Therapeutic Opportunities," <u>Trends in Pharmacological Sciences</u> , 13:108-113 (1992).	
	CZ	<i>Gene Targeting A Practical Approach</i> , edited by Joyner, A.L., Oxford Univ. Press (1993) cover page & table of contents.	
	DA	Glenner et al. "Alzheimer's disease: Initial report of the purification and characterization of a novel cerebrovascular amyloid protein" <u>Biochem. Biophys. Res. Comm.</u> , 120:885-890 (1984).	
	DB	Glenner et al., "Alzheimer's disease and Down's Syndrome: Sharing of unique cerebrovascular amyloid fibril protein" <u>Biochem. Biophys. Res. Comm.</u> , 122:1131-1135 (1984).	
	DC	Goate et al., "Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease" <u>Nature</u> , 349:704-706 (1991).	
	DD	Goding, James W., "Production and application of monoclonal antibodies in cell biology, biochemistry and immunology" in: <u>Monoclonal Antibodies: Principles and Practice</u> , Ch. 3, pp. 56-74, <u>Academic Press</u> , London (1984).	
	DE	Golde et al., "Processing of the amyloid protein precursor to potentially amyloidogenic derivatives" <u>Science</u> , 255:728-730 (1992).	

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	DF	Golde et al., "Production of Amyloid $\beta$ Protein from Normal Amyloid $\beta$ -Protein Precursor ( $\beta$ APP) and the Mutated $\beta$ APPs Linked to Familial Alzheimer's Disease," from <i>Alzheimer's Disease Amyloid Precursors Proteins, Signal Transduction, and Neural Transplantation</i> , vol. 695, pgs. 103-108, by Annals of the New York Academy of Sciences (1993).	
	DG	Goldgaber et al., "Characterization and Chromosomal Localization of a cDNA Encoding Brain Amyloid of Alzheimer's Disease," <i>Science</i> , 235:877-880 (1987).	
	DH	Goverman et al., "Transgenic Mice That Express a Myelin basic Protein-Specific T Cell Receptor Develop Spontaneous Autoimmunity," <i>Cell</i> , 72:551-560 (1993).	
	DI	Greaves et al., "A transgenic mouse model of sickle cell disorder," <i>Nature</i> , 343:183-185 (1990).	
	DJ	Greenberg et al., "Transgenic Mouse Studies of Alzheimer Amyloid Precursor (APP) Proteins and Derivatives," <i>Society for Neuroscience Abstracts</i> , vol. 18 part2, abstract 616.7 (1992).	
	DK	Greenberg et al., "Yet More Transgenic Mouse Studies of Alzheimer Amyloid Precursor (APP)," <i>Soc. for Neurosci. Abstracts</i> , 19:1035, abst. 421.12 (1993).	
	DL	Haass et al., "Amyloid $\beta$ -peptide is produced by cultured cells during normal metabolism" <i>Nature</i> , 359:322-325 (1992).	
	DM	Haass et al., "Cellular Processing of $\beta$ -Amyloid Precursor Protein and the Genesis of Amyloid $\beta$ -Peptide," <i>Cell</i> , 75:1039-1042 (1993).	
	DN	Hammer et al., "Partial correction of murine hereditary growth disorder by germ-line incorporation of a new gene," <i>Nature</i> , 311:65-67 (1984).	
	DO	Hardy et al., "The Alzheimer family of diseases: many etiologies, one pathogenesis?," <i>PNAS</i> , 94:2095-2097 (1997).	
	DP	Hardy, J., "Framing $\beta$ -amyloid," <i>Nature Genetics</i> , 1:233-234 (1992).	
	DQ	HARRIS et al., "Transgenic Animals as Tools in Drug Development," <i>Agents &amp; Actions</i> (38) Special Conference Issue, 1993.	
	DR	Hendricks et al., "Presenile dementia and cerebral haemorrhage linked to a mutation at codon 692 of the $\beta$ -amyloid precursor protein gene," <i>Nature Genetics</i> , 1:218-221 (1992).	

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First Named Inventor	McLonlogue, Lisa C., et. al.
Art Unit	1632
Examiner Name	Crouch, D.

Attorney Docket Number 015270-012100US

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	DS	Higgins et al., "Transgenic mice expressing human $\beta$ -APP751, but not mice expressing $\beta$ -APP695, display early Alzheimer's disease-like histopathology" <i>Annals NY Acad. Sci.</i> , 695:224-227 (1993).	
	DT	Higgins et al., "Transgenic mouse brain histopathology resembles early Alzheimer's disease" <i>Ann. Neurol.</i> , 35:598-607 (1994).	
	DU	Hogan et al., <i>Manipulating the Mouse Embryo, A Laboratory Manual</i> , Cold Spring Harbor Laboratory, (1986) cover page and table of contents.	
	DV	Holtzman et al., "Molecular studies in Alzheimer's disease," <i>TIBS</i> , 16:140-144 (1991).	
	DW	Howland et al., "Neuron-Specific Expression of Human Beta-Amyloid Precursor Protein (APP) In Transgenic Mice," <i>Society for Neuroscience Abstracts</i> , 19:1035, abstract 421.13 (1993).	
	DX	Hsiao et al., "Spontaneous Neurodegeneration in Transgenic Mice with Mutant Prion Protein," <i>Science</i> , 250:1587-1590 (1990).	
	DY	Hyman et al., "Amyloid, dementia and Alzheimer's disease," <i>Curr. Opin. Neurology Neurosurgery</i> , 5:88-92 (1992).	
	DZ	Hyman et al., "Kunitz protease inhibitor-containing amyloid $\beta$ -protein precursor immunoreactivity in Alzheimer's disease" <i>J. Neuropath. Exp. Neurol.</i> , 51:76-83 (1992).	
	EA	Iwamoto et al., "Neuroblastoma in a transgenic mouse carrying a metallothionein/ <i>ret</i> fusion gene," <i>Br. J. Cancer</i> , 67:504-507 (1993).	
	EB	Jan et al., "Receptor-regulated ion channels," <i>Curr. Opin. Cell Biology</i> , 9:155-160 (1997).	
	EC	Jones et al., "Mutation in codon 713 of the $\beta$ amyloid precursor protein gene presenting with schizophrenia," <i>Nature Genetics</i> , 1:306-309 (1992).	
	ED	Kammesheidt et al., "Deposition of $\beta$ /A4 immunoreactivity and neural pathology in transgenic mice expressing the carboxyl-terminal fragment of the alzheimer Amyloid precursor in the brain," <i>PNAS</i> , 89:10857-10861 (1992).	
	EE	Kang et al., "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor" <i>Nature</i> , 325:733-736 (1987).	
	EF	Keffer et al., "Transgenic mice expressing human tumor necrosis factor: a predictive genetic model of arthritis," <i>EMBO J.</i> , 10(13):4025-4031 (1991).	

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	EG	Kennedy et al., "Familial Alzheimer's disease," <u>Brain</u> , 116:309-324 (1993).	
	EH	Kennedy et al., "Only Kunitz-inhibitor-containing isoforms of secreted Alzheimer amyloid precursor protein show amyloid immunoreactivity in normal cerebrospinal fluid" <u>Neurodegeneration</u> , 1:59-64 (1992).	
	EI	Kitaguchi et al., "Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity" <u>Nature</u> , 331:530-532 (1988).	
	EJ	Koliatsos et al., "Neurotrophic Strategies for Treating Alzheimer's Disease: Lessons from Basic Neurobiology and Animal Models," from <u>Alzheimer's Disease Amyloid Precursor Proteins, Signal Transduction, and Neural Transplantation</u> , vol. 695, pgs. 292-299, by Annals of the New York Academy of Sciences (1993).	
	EK	Konig et al., "Identification and Differential Expression of a Novel Alternative Splice Isoform of the $\beta$ A4 Amyloid Precursor Protein (APP) mRNA in Leukocytes and Brain Microglial Cells," <u>J. Biol. Chem.</u> , 267(15):10804 (1992).	
	EL	Korf et al., "S-Antigen and Rod-Opsin Immunoreations in Midline Brain Neoplasms of Transgenic Mice: Similarities to Pineal Cell Tumors and Certain Medulloblastomas in Man," <u>J. Neuropath. Exper. Neuology</u> , 49(4):424-437 (1990).	
	EM	Kozak, M., "The Scanning Model for Translation: An Update," <u>J. Cell Biology</u> , 108:229-241 (1989).	
	EN	Kozlowski et al., "the Neurotoxic Carboxy-Terminal Fragment of the Alzheimer Amyloid Precursor Binds Specificity to a Neuronal Cell Surface Molecule: pH Dependence of the Neurotoxicity and the Binding," <u>J. Neuroscience</u> , 12(5):1679-1687 (1992).	
	EO	Lamb et al., "Introduction and expression of the 400 kilobase <i>precursor amyloid protein</i> gene in transgenic mice," <u>Nature Genetics</u> , 5:22-30 (1993).	
	EP	Lannfelt et al., "Low frequency of the APP 670/671 mutation in familial Alzheimer's disease in Sweden," <u>Neuroscience Letters</u> , 153:85-87 (1993).	
	EQ	Lavigne et al., "High Incidence of Lung, Bone, and Lymphoid Tumors in Transgenic Mice Overexpressing Mutant Alleles of the p53 Oncogene," <u>Mol. Cellular Biol.</u> , 9(9):3982-3991 (1989).	
	ER	Levy et al., "Mutation of the Alzheimer's Amyloid Gene in Hereditary Cerebral Hemorrhage, Dutch Type," <u>Science</u> , 248:1124-1126 (1990).	
	ES	Lieberburg et al., "Expression of Human Alzheimer's Amyloid Precursor Protein In Transgenic Mice," <u>Soc. Neuroscience Abstracts</u> , vol. 19, abstract 421.15 (1993).	

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	ET	Luo et al., "Human Amyloid Precursor Protein Behavior Deficit of Flies Deleted for Appl Gene," <u>Neuron</u> , 9:595-605 (1992).	
	EU	Marx, J., "Alzheimer's Research Moves to Mice," <u>Science</u> , 253:266-267 (1991).	
	EV	Marx, J., "Major Setback for Alzheimer's Models," <u>Science</u> , 255:1200-1202 (1992).	
	EW	Marx, J., "New Lead to an Alzheimer's Mouse?," <u>Science</u> , 261:1520 (1993).	
	EX	MERLINO, Glenn T., "Transgenic Animals in Biomedical Research," <u>Faseb J</u> , 5:2996-3001.	
	EY	Miller et al., "Alzheimer's disease: transgenic models to test new chemicals and pharmaceuticals," <u>Curr. Opin. Biotechnology</u> , 3:683-686 (1992).	
	EZ	Moran et al., "Age-related learning deficits in transgenic mice expressing the 751-amino acid isoform of human $\beta$ -amyloid precursor protein," <u>PNAS</u> , 92:5341-5345 (1995).	
	FA	Mullan et al., "A pathogenic mutation for probable Alzheimer's disease in the APP gene at the N-terminus of $\beta$ -amyloid" <u>Nature Genetics</u> , 1:345-347 (1992).	
	FB	Mullan et al., Genetic and molecular advances in Alzheimer's disease," <u>TINS</u> , 16(10):398-403 (1993).	
	FC	Mullan, M., "Familial Alzheimer's disease: second gene locus located," <u>BMJ</u> , 305:1108-1109 (1992).	
	FD	Mullins et al., "Fulminant hypertension in transgenic rats harbouring the mouse <i>Ren-2</i> gene," <u>Nature</u> , 344:541-544 (1990).	
	FE	Murrell et al., "A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease" <u>Science</u> , 254:97-99 (1991).	
	FF	NARISAWA et al., "Transgenic Mice Expressing the Tumor Marker Germ Cell Alkaline Phosphatase: An In Vivo Tumor Model for Human Cancer Antigens," <u>PNAS</u> , 90:5081-5085 (1993).	
	FG	Neve et al., "Brain transplants of cells expressing the carboxyl-terminal fragment of the Alzheimer amyloid protein precursor cause specific neuropathology <i>in vivo</i> ," <u>PNAS</u> , 89:3448-3452 (1992).	

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	FH	Nussbaum et al., "Alzheimer's Disease and Amyloid Protein – in (Transgenic) Mice and Men," <u>Harefuah</u> , 123(9):362-364, document in Hebrew (1992).			
	FI	Oltersdorf et al., "The Alzheimer's amyloid precursor protein: Identification of a stable intermediate in the biosynthetic/degradative pathway" <u>J. Biol. Chem.</u> , 265:4492-4497 (1990).			
	FJ	Oltersdorf et al., "The secreted form of the Alzheimer's amyloid precursor protein with the Kunitz domain is protease nexin-II" <u>Nature</u> , 341:144-147 (1989).			
	FK	Order Denying Mayo's Ex Parte Motion to Stay Deadline for Motion for Attorney's Fees, US District Court for the Northern District of California, Case No. C99-04464 WHA.			
	FL	Order Granting Defendant's Motion for Summary Judgment of Anticipation, US District Court for the Northern District of California, Case No. C99-04464 WHA.			
	FM	Palmert et al., "Soluble derivatives of the $\beta$ amyloid protein precursor of Alzheimer's disease are labeled by antisera to the $\beta$ amyloid protein" <u>Biochem. Biophys. Res. Comm.</u> , 165:182-188 (1989).			
	FN	Palmert et al., "The $\beta$ -amyloid protein precursor of Alzheimer's disease has soluble derivatives found in human brain and cerebrospinal fluid" <u>Proc. Natl. Acad. Sci.</u> , USA 86:6338-6342 (1989).			
	FO	Palmiter et al., "Dramatic growth of mice that develop from eggs microinjected with metallathionein-growth hormone fusion genes," <u>Nature</u> , 300:611-615 (1982).			
	FP	Palvin, R., "Brain Amyloid in Alzheimer's Disease – A New Experimental Model," <u>Neurologia Croatica</u> , 41(4):227-234 (1992).			
	FQ	Pearson et al., "Expression of the human $\beta$ -amyloid precursor protein gene from a yeast artificial chromosome in transgenic mice," <u>PNAS</u> , 90:10578-10582 (1993).			
	FR	Perraud et al., "The promoter of the human cystic fibrosis transmembrane conductance regulator gene directing SV-40 T antigen expression induces malignant proliferation of ependymal cells in transgenic mice," <u>Oncogene</u> , 7:993-997 (1992).			
	FS	Ponte et al., "A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors" <u>Nature</u> , 331:525-527 (1988).			
	FT	Price et al., "Alzheimer's Disease-Type Brain Abnormalities in Animal Models," <u>Down Syndrome and Alzheimer Disease</u> , pgs. 271-287, Wiley-Liss, Inc., (1992).			
	FU	Pullian et al., "Use of aggregating brain cultures to study the replication of herpes simplex virus types 1 and 2 in central nervous system tissue" <u>J. Virol. Met.</u> , 9:301-316 (1984).			
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	FV	Quon et al., "Formation of $\beta$ -amyloid deposits in brains of transgenic mice" <i>Nature</i> , 352:239-241 (1991).	
	FW	Quon et al., "Formation of $\beta$ -amyloid protein deposits in brains of transgenic mice," <i>Nature</i> , 352:239-241 (1991).	
	FX	Roakis et al., "An alternative secretase cleavage produces soluble Alzheimer amyloid precursor protein containing a potentially amyloidogenic sequence" <i>Soc. Neurosci.</i> , Abstract No. 15.5 (Oct. 26, 1993) Anaheim, CA.	
	FY	Robakis et al., "Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides," <i>PNAS</i> , 84:4190-4194 (1987).	
	FZ	Roche et al., "Biologically Active Domain of the Secreted Form of the Amyloid $\beta$ /A4 Protein Precursor," from <i>Alzheimer's Disease Amyloid Precursor Proteins, signal Transduction, and Neuronal Transplantation</i> , Annals of the New York Academy of Sciences, vol. 695, pgs. 149-157 (1993).	
	GA	Ryan et al., "Human Sickle Hemoglobin in Transgenic Mice," <i>Science</i> , 247:566-568 (1990).	
	GB	Sahasrabudhe et al., "Release of Amino-terminal Fragments from Amyloid Precursor Protein Reporter and Mutated Derivatives in Cultured Cells," <i>J. Biol. Chemistry</i> , 267(15):25602-25608 (1992).	
	GC	Sandhu et al., "Expression of the Human $\beta$ -Amyloid Protein of Alzheimer's Disease Specifically in the Brains of Transgenic Mice," <i>J. Biol. Chemistry</i> , 266(32):21331-21334 (1991).	
	GD	Sarvetnick et al., "Insulin-Dependant diabetes Mellitus Induced in Transgenic Mice by Ectopic Expression of Class II MHC and Interferon-Gamma," <i>Cell</i> , 52:773-782 (1988).	
	GE	Savage et al., "Human Amyloid Precursor Protein Expression in Transgenic Mice as a Model of Alzheimer's Disease: Search for pathology," abstract 421.14, <i>Society for Neuroscience Abstracts</i> , 19:1035 (1993).	
	GF	Scott et al., "Inability to Detect $\beta$ -Amyloid Protein Precursor mRNA in Alzheimer Plaque-Associated Microglia," <i>Experimental Neurology</i> , 121:113-118 (1993).	
	GG	Scott et al., "The Processing of Native and Mutant APP751 in Human 293 Cells," <i>Neurobiology of Aging</i> , 13(supp. 1):578-579, abstract 310 (1992).	
	GH	Scott et al., "Transgenic Mice Expressing Hamster Prion Protein Produce Species-Specific Scrapie Infectivity and Amyloid Plaques," <i>Cell</i> , 59:847-857 (1989).	

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	GI	Selkoe et al., "Physiological production of the $\beta$ -amyloid protein and the mechanisms of Alzheimer's disease" <i>Trends Neurosci.</i> , 16 (10):403-409 (Oct. 1993).	
	GJ	Selkoe et al., "Physiological production of the $\beta$ -amyloid protein and the mechanism of Alzheimer's disease," <i>Trends in Neuroscience</i> , 16(10):403-409 (1993).	
	GK	Selkoe et al., " $\beta$ -amyloid precursor protein of Alzheimer disease occurs as 110- to 135-kilodalton membrane-associated proteins in neural and nonneural tissue" <i>Proc. Natl. Acad. Sci.</i> , USA 85:7341-7345 (1988).	
	GL	Seubert et al., "Isolation and quantification of soluble Alzheimer's $\beta$ -peptide from biological fluids" <i>Nature</i> , 359:325-327 (1992).	
	GM	Seubert et al., "Secretion of $\beta$ -amyloid precursor protein cleaved at the amino terminus of the $\beta$ amyloid peptide" <i>Nature</i> , 361:260-263 (1993).	
	GN	Siman et al., "Processing of the $\beta$ -Amyloid Precursor Multiple Proteases Generate and Degrade Potentially Amyloidogenic Fragments," <i>J. Biol. Chemistry</i> , 268(22):16602-16609 (1993).	
	GO	Sisodia, S.S., " $\beta$ -Amyloid precursor protein cleavage by a membrane-bound protease," <i>PNAS</i> , 6075-6079 (1992).	
	GP	Society for Neuroscience, Abstracts, Volume 19, Part 2, 23 <sup>rd</sup> Annual Meeting, Washington, DC, November 7-12, 1993.	
	GQ	Society for Neuroscience Abstracts, Volume 18, Part 2, 22 <sup>nd</sup> Annual Meeting, Anaheim, California, October 25-30, 1992	
	GR	Sofroniew et al., "Transgenic modelling of neurodegenerative events gathers momentum," <i>TINS</i> , 14(12):513 (1991).	
	GS	Stacey et al., "Perinatal lethal osteogenesis imperfecta in transgenic mice bearing an engineered mutation pro- $\alpha$ 1(I) collagen gene," <i>Nature</i> , 332:131-136 (1988).	
	GT	Stout et al., "Expression of human HPRT in the central nervous system of transgenic mice," <i>Nature</i> , 317:250 (1985).	
	GU	Supplement 1 to Volume 15 of Journal "Neurobiology of Aging", Research on Age-Related Phenomena, Neurodegeneration and Neuropathology, Abstract 49.	
	GV	Tanzi et al., "Amyloid $\beta$ Protein Gene:cDNA, mRNA Distribution, and Genetic Linkage Near the Alzheimer Locus," <i>Science</i> , 235:880-884 (1987).	

Examiner Signature	Date Considered
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Application Number	Unassigned
Filing Date	Herewith
First Named Inventor	McLonlogue, Lisa C., et. al.
Art Unit	1632
Examiner Name	Crouch, D.

Attorney Docket Number 015270-012100US

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	GW	Tanzi et al., "Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease," <u>Nature</u> , 331:528-530 (1998).	
	GX	Tomita et al., "The presenilin 2 mutation (N141I) linked to familial Alzheimer disease (Volga German families) increases the secretion of amyloid $\beta$ protein ending at the 42nd (or 43rd) residue," <u>PNAS</u> , 94:2025-2030 (1997).	
	GY	Travis, J., "New Piece in Alzheimer's Puzzle," <u>Science</u> , 261:828-829 (1993).	
	GZ	Travis, J., "New Piece in Alzheimer's Puzzle," <u>Science</u> , 261:828-829 (1993).	
	HA	Usami et al., "The Triplet of Lysine Residues (Lys724-Lys725-Lys726) of Alzheimer's Amyloid Precursor protein Plays an Important Role in membrane Anchoage and Processing," <u>J. Neurochem.</u> , 61(1):239-246 (1993).	
	HB	Van Duijn et al., "Genetic transmission of Alzheimer's disease among families in a Dutch population based study," <u>J. Med. Genet.</u> , 30:640-646 (1993).	
	HC	Wang et al., "Tissue- and Development-specific Expression of the Human Phenylalanine Hydroxylase/Chloramphenicol Acetyltransferase Fusion Gene in Transgenic Mice," <u>J. Biological Chemistry</u> , 267(21):15105-15110 (1992).	
	HD	Weidemann et al., "Identification, biogenesis, and localization of precursors of Alzheimer's disease A4 amyloid protein" <u>Cell</u> , 57:115-126 (1989).	
	HE	Wells et al., "Human dystrophin expression corrects the myopathic phenotype in transgenic mdx mice," <u>Human Molecular Genetics</u> , 1(1):35-40 (1992).	
	HF	Westphal, H., "Mouse models of human disease," <u>Curr Opin. Biotech.</u> , 2:830-833 (1991).	
	HG	Wiedlocha et al., "Dual Mode of signal Transduction by Externally Added Acidic Fibroblast Growth Factor," <u>Cell</u> , 76:1039-1051 (1994).	
	HH	Wirak et al., "Age-Associated Inclusions in Normal and Transgenic Mouse Brain," <u>Science</u> , 255:1443-45 (1992).	
	HI	Wirak et al., "Deposits of Amyloid $\beta$ Protein in the Central Nervous system of Transgenic Mice," <u>Science</u> , 253:323-325 (1991).	

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	HJ	Wirak et al., "Regulatory region of human amyloid precursor protein (APP) gene promotes neuron-specific gene expression in the CNS of transgenic mice," <u>EMBO</u> , 10(2):289-296 (1991).	
	HK	Yamaguchi, "Transgenic mice for the amyloid precursor protein 695 isoform have impaired spatial memory," <u>NeuroReport</u> , 2(12):781-784 (1991).	
	HL	Yanker et al., "Neurotoxicity of a Fragment of the Amyloid Precursor Associated with Alzheimer's Disease," <u>Science</u> , 245:417-420 (1989).	

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